Allergy Abstracts

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Asthma and Hay Fever

The Use of Oral Compound F (17-Hydroxycorticosterone) in Asthma. Fyles, T. W., and Rose, B.: Canad. M. A. J. **70**: 642, 1954.

Oral Compound F was administered to fifteen patients with bronchial asthma. In patients who previously had been taking cortisone, the 20 mg. hydrocortisone tablets were substituted for the 25 mg. cortisone tablets without the patients' knowledge. Some patients who had not previously received hormone therapy were also studied. The patients, who were all fairly ill, were ambulatory cases ranging in age from 6 to 59 years. About 50 per cent of the patients responded within the first twenty-four hours; the remainder were improved within the next forty-eight hours. The initial twenty-four

hour dose of hydrocortisone averaged about 160 mg., while the maintenance dose varied from 20 to 80 mg. daily. The duration of relief obtained following cessation of hydrocortisone therapy was studied in five cases and was found to last from seven to ninety days. The effect of hydrocortisone upon the eosinophil count was found to be roughly comparable to that of cortisone. Urinary steroid excretion was measured in two patients and was found to be similar to that of patients on cortisone. Side effects were minimal. The patients were not placed on strict low-salt diets. Satisfactory results were obtained with a dose of Compound F approximately 20 per cent lower than the required dose of cortisone. The authors suggest that hydrocortisone is equally as effective as cortisone in the treatment of bronchial asthma and, milligram for milligram, is probably a more effective therapeutic agent for this disease. They emphasize, however, that none of the hormones offers more than temporary relief and that hormone therapy should be employed only in those cases where standard forms of allergic management have been unsuccessful.

R. W.

The Use of a Suspension of Cortogen Acetate With Chlor-Trimeton Maleate in the Treatment of Allergic Rhinitis of Pollen Origin. Evans, W. H.: Tr. Am. Acad. Ophth. **58**: 89, 1954.

A series of seventy-seven patients with allergic rhinitis caused by ragweed or grass pollens was treated with topical applications of a Cortogen-Chlor-Trimeton suspension containing cortisone in 5 per cent and Chlor-Trimeton in 2.5 per cent concentrations. A thin cotton pledget saturated with the Cortogen-Chlor-Trimeton mixture was placed against the nasal septum for forty-five minutes and then against the lateral nasal wall for a similar period of time. Nose drops of the suspension were used every two or three hours. In about 10 per cent of the patients, burning or irritation of the nasal mucosa occurred. The majority of the patients reported considerable relief with this therapy.

M. C.

Dermatology

Treatment of Eczema With Cortisone Ointment. Hermann, V.: Arch. Dermat. & Syph. **68**: 525, 1953.

In order to evaluate the effectiveness of cortisone ointment in the treatment of eczema, thirty-five children with eczema were studied for periods ranging from one to four weeks. Cortisone, dissolved in various bases, was applied to one affected area on the body, while the ointment base alone was applied to a contralateral surface. The cortisone was always applied to the area most heavily involved. In many of the clinical trials, chloroform, an excellent solvent for cortisone, was used to dissolve the cortisone before it was incorporated into the ointment base. The author's evaluation of results was confirmed by impartial observers. About 45 per cent of the youngsters showed improvement on this treatment, 50 per cent were unimproved, and 5 per cent were worse. The use of chloroform as a solvent for the cortisone proved to have no particular advantage over other solvents. The maximum amount of cortisone applied locally to any patient's skin in one day was 55 mg., while the average amount was less than 20 mg. Eosinophil counts showed that not enough cortisone was absorbed into the blood stream to produce a systemic effect. Relapses quickly followed cessation of therapy in most cases. The author is of the opinion that local cortisone is probably ineffective because not enough of the hormone is able to penetrate into the dermal tissue. He concludes that local cortisone therapy is no more effective than conventional dermatological management in treating eczema.

R. W.

Atopic Dermatitis. A Study of Its Natural Course and of Wool As a Dominant Allergenic Factor. Osborne, E. D., and Murray, P. F.: Arch. Dermat. & Syph. **68**: 619, 1953.

The authors studied the records of more than 2,500 patients of all ages. The rashes observed in youngsters under 1 year of age were found to be due to external causes in 30 to 40 per cent of the cases. External medication and contact with alkalies were the agents most often responsible for the dermatitis. The rash started during the seven cold months (September through March) in 75 per cent of 500 infants under 2 years of age and in 82 per cent of 300 children from 5 to 10 years of age. Seventy-five per cent of 300 children between the ages of 2 and 5 had no dermatitis or were much improved during the summer.

The authors are of the opinion that wool fiber by contact or by inhalation is the chief cause of atopic dermatitis. Of 89 patients with chronic atopic dermatitis followed for 5 to 26 years, wool was shown by skin test and by clinical trial to be the dominant allergic factor in about two-thirds of the cases. Of 76 patients who were sent to southern Florida, about 90 per cent reported satisfactory progress while in the South; exacerbation of the rash occurred when they returned north during the cold weather. The authors studied the amount of wool fibers found in the house dusts of their patients. A technique was developed for collecting the dust and staining the fibers with Millon's reagent on a glass slide. The examination of routine house dusts in Buffalo revealed an average wool content of 5 to 50 per cent. When dust from the same environs was examined during the summer months, the percentage of wool fiber dropped to 1 or 2 per cent, with a maximum of 5 per cent. Removal of all woolen products from the house reduced the wool fiber content in the house dust to 1 or 2 per cent. Dust from modern schools with filtered air contained only 1 or 2 per cent of wool fiber. To protect a patient against wool fiber, all wool rugs, carpets, blankets, and fuzzy wool clothing should be removed and an electric filtering mechanism should be installed in the patient's home. Three cases were discussed in detail to illustrate these points. Microscopic examinations of the house dust are recommended in order to determine the percentage of wool fiber in the patient's environment and to control the proper avoidance of the exposure to wool.

R. W.

Use of Oral Procaine in Control of Pruritus. Beinhauer, L. G.: Arch. Dermat. & Syph. **69**: 188, 1954.

Procaine hydrochloride was administered orally in combination with ascorbic acid to 145 patients suffering from pruritus. The causes of the pruritus were classified under twenty-three different categories. The medication was given in capsules, each containing 250 mg. of powdered procaine hydrochloride and 150 mg. of granular ascorbic acid. The ascorbic acid was added to the treatment program since it had seemed to potentiate the intravenous action of procaine in relieving pruritus. Each patient received two capsules initially and then one capsule every three hours for the next two days. The dosage then was gradually reduced during the next seven to fourteen days.

Relief was often obtained within four days in cases of urticaria due to penicillin sensitivity. In other urticarias and in nummular eczema, there was no improvement. In four of ten cases of generalized neurodermatitis, there was some temporary relief. Improvement usually occurred rapidly or not at all. Patients with herpes zoster or burning tongue responded well, but the results in most of the other conditions were equivocal. When intravenous procaine had failed to help, no benefit was obtained from oral therapy. Relief

lasted from a few days to a few months. Reactions occurred in 8 per cent of the patients and consisted of headache, dizziness, nausea, vomiting, or drowsiness. Oral procaine is recommended as safe medication which may give relief of pruritus when other methods fail. However, it does not appear to offer any pronounced advantage over the more conventional methods of treating pruritus.
R. W.

Oral Hyposensitization by Oleoresin Extracts. Brachman, B., and Roy, A. K.: Canad. M. A. J. **71**: 4, 1954.

Nineteen patients with plant contact dermatitis were treated by the oral administration of the specific oleoresin extract. Sixteen of these patients were patch tested and eighteen were scratch tested with oleoresin extracts from the common local weeds, grasses, trees, and flowers. The open method of patch testing was employed, the material being allowed to dry on the skin. Nine of the seventeen patients patch tested in this manner had positive reactions and five of the patients had positive scratch reactions (protein-sensitive). All patients were given oral oleoresin therapy, regardless of the results of their skin tests. The oleoresins were administered in gradually increasing amounts, beginning with a 1:100 dilution and working up to the 1:25 dilution. The material was administered in gelatin capsules for a period of from two to eight months. The most common complication of treatment was pruritus ani; some patients also experienced mild urticaria. If an untoward reaction occurred, treatment was interrupted temporarily and the dosage was usually decreased when therapy was reinstituted. The results of treatment were evaluated on the basis of replies to questionnaires answered by the patients. Six out of nine oleoresin contact-sensitive patients under therapy for at least one year showed definite improvement. Of five protein-sensitive patients, two reported improvement; one of the two appeared also to have a sensitivity of the contact type. Five patients stopped their treatment because of side reactions or a flare-up of their skin conditions. The authors conclude that oral hyposensitization is of benefit in the treatment of plant dermatitis due to oleoresin contact sensitivity. It is not of benefit in patients sensitive to the protein fraction of the plant.
R. W.

Low Incidence of Dermographism in Subacute and Chronic Urticaria. Fisher, A. A., and Schwartz, S.: Arch. Dermat. & Syph. **68**: 553, 1953.

One hundred patients with nonurticarial dermatoses were examined for the presence of dermographism. Five demonstrated a typical dermographic response. One hundred patients with subacute or chronic urticaria were similarly examined, and six of them were found to have dermographism. These patients were tested while they were having urticaria. In only 19 per cent of the patients was the urticaria considered to be allergic in origin. The etiological mechanism in the remaining eighty-one patients was unknown. The author concludes that there is no relationship between chronic urticaria and dermographism and that dermographism is not caused by an allergic mechanism.
R. W.

Personality Factors in Adult Atopic Eczema. McLaughlin, J. T., Shoemaker, R. J., and Guy, W. B.: Arch. Dermat. & Syph. **68**: 506, 1953.

A group of nine male and twenty-one female patients with severe atopic dermatitis was studied jointly by a dermatologist and a group of psychiatrists. Careful social situation appraisals were made by a social worker, including interviews with other members of the patient's family. Twenty-seven of these

patients were evaluated on the basis of psychological tests, consisting of the Wechsler-Bellevue intelligence scale, the Rorschach test, and the thematic apperception test. About one-half of the patients had a positive family history of allergy. The authors summarized their description of the typical patient with eczema as follows: "A long-standing personality disorder characterized by great passivity and excessive concern over acceptance by others, a deep but distrustful dependence upon a parental figure, a chronic, seething hostility over repeated failure to obtain consistent dependent satisfactions from this person or anyone else, and an over-all inhibition of healthy aggressiveness. . . . While more assertive persons would react by taking action to solve or diminish the stress situation, these patients tend to itch and scratch in fuming inactivity."

The authors conclude that atopic eczema is a psychophysiologic skin disorder which occurs in conjunction with primitive polymorphous personality patterns. They state further that these personality patterns are not unique to eczema but are commonly found in other diseases, such as arthritis, hypertension, colitis, and asthma. R. W.

Allergic Eczematous Contact-Type Dermatitis Due to Zoris. Lazar, M. P.: Arch. Dermat. & Syph. **69**: 104, 1954.

An American soldier stationed in Japan developed an erythematous vesicular eruption on his feet, which subsequently spread to his hands. Zoris was suspected as the cause of the eruption. Zoris is a special type of open shoe worn in Japan as a house or shower slipper. They are made of rubber, rice, straw, leather, and wood, plus additional materials used as retaining straps. The rash on the hands developed five days after the appearance of the initial lesions on the feet. Conventional patch tests on the patient elicited a positive response to the rubber material used in making the zoris and showed negative reactions on several controls. The author stresses the fact that it is not customary to touch the zoris when putting them on the feet and wonders whether this patient may have developed the rash on his hands by hematogenous spread. R. W.

Otorhinology and Ophthalmology

Ocular Manifestations in Löffler's Syndrome. Velzeboer, C. M. J.: Brit. J. Ophth. **37**: 731, 1953.

A 37-year-old woman was hospitalized because of haziness and veil before the right eye for three days. She had had a previous similar experience but symptoms disappeared within thirty minutes. There was a past history of bronchitis in childhood and recent episodes of shortness of breath and wheezing. The patient had had encephalitis about ten years previously. Her mother had vasomotor rhinitis.

The only significant physical finding was a whitish infiltration involving the innermost layers of the retina of the right eye. The surrounding area appeared grayish and edematous. The blood count showed a 46 per cent eosinophilia. An x-ray picture of the chest was normal. Routine skin tests with allergens gave negative reactions. Stool examinations were negative for intestinal parasites.

Within the next few weeks, the infiltrate in the retina subsided, but new infiltrations appeared in other areas. Because of the fugitive character of the retinal infiltrates and the continued high blood eosinophilia, the diagnosis of Löffler's syndrome was considered and repeated x-ray pictures of the chest

were taken. About two weeks after admission, shadows appeared on the left lung which gradually decreased in size and disappeared after one week. During the next three months, the retinal infiltrates gradually subsided and two cicatrices remained in the right fundus. Associated visual field defects were demonstrated. A visual field defect was also detected in the left eye where no infiltration was found, indicating a local affection of the left optic nerve. The blood eosinophilia persisted for more than a year after the processes in the retina and lung healed.

The author points out that this is the first report of localization of an infiltrate in the eye in Löffler's syndrome. He also calls attention to the fact that, although the lesions in Löffler's syndrome are generally reversible, more severe and permanent lesions may result. B. S.

Intranasal Corticotrophin in Hay Fever and Allergic Rhinitis. Schwarz, H.: Canad. M. A. J. **71**: 128, 1954.

Thirteen patients with various types of nasal allergies were treated with intranasal insufflations of corticotrophin. Bacitracin and tyrothricin were added to the powdered hormone in order to increase the effectiveness of the mixture in relieving infected nasal mucous membranes. Placebo sprays, which were administered to five patients for three days prior to the institution of hormone therapy, were found to be totally ineffective. The patients received from 40 to 100 units in divided doses initially. Twenty units were usually administered at each individual treatment. The effective maintenance dose varied from 5 to 20 units daily. Patients were treated for several weeks during the height of the ragweed season in order to evaluate this type of therapy. An indicator with a bittersweet taste was added to the hormone powder to make certain that the latter was being deposited properly on the nasal mucous membrane rather than being absorbed by the mucous membranes of the nasopharynx. Every patient reported a complete remission of symptoms following the intranasal hormone therapy regardless of whether he was suffering from simple hay fever, perennial rhinitis, nasal polyposis, or chronic sinusitis. One patient developed an allergic reaction to the antibiotics, another became sensitized to the hormone spray, and a third person developed mental changes. It was necessary to stop treatment in three of the thirteen patients because of side reactions. Even though nasal polyps completely disappeared with treatment, the author stresses the fact that the benefits obtained from this mode of therapy are only temporary in nature. He further emphasizes the need for taking the same precautions to prevent side reactions during intranasal hormone therapy that are employed in parenteral hormone therapy. R. W.

Some Uses of Antihistamine in Defective Hearing Due to Allergy. Armstrong, C. W.: Tr. Am. Acad. Ophth. **58**: 104, 1954.

An audiologic test was devised to determine whether allergic factors were causing defective hearing. Audiograms for air and bone conduction were made in suspected patients. Following an injection of 10 mg. of Chlor-Trimeton, a second audiogram was made thirty minutes later. A significant gain in hearing following the injection of antihistamine was considered evidence that there was an allergic cause for the deafness. In such cases, allergic management, including skin testing, was instituted. In the process of desensitization the addition of antihistamine to the allergen tended to produce more rapid improvement in allergic deafness than treatment with the antigen alone. M. C.

Common Manifestations of Allergy in Ophthalmology. Lemoine, A. N., Sr.: Tr. Am. Acad. Ophth. **58**: 125, 1954.

Among allergic conditions affecting the eye, several diseases of the cornea were discussed. A small percentage of cases of phlyctenular keratitis and interstitial keratitis were attributed to air-borne antigens or to foods. Small, superficial, punctate ulcers frequently were attributed to contact allergens or to foods. Severe ulcerations may result from the use of dyes for hair, eyebrows, or eyelashes. The author reported the case of a patient with a dendritic ulcer which always recurred following the ingestion of chocolate.

M. C.

Non-surgical Management of Ménière's Disease. Derlacki, E. L.: Laryngoscope **64**: 271, 1954.

In a study of fifty-five cases of Ménière's disease, six proved to have an allergic etiology. In one case, complete relief of symptoms followed the elimination of milk; in another, sensitivity to house dust was an important factor. Allergic patients responded well to treatment.

In nonallergic patients, nonspecific medical management, consisting of low-salt diets, potassium chloride, and subcutaneous injections of small doses of histamine, was tried. Satisfactory results were obtained in a majority of patients on this regime. M. C.

Use of Cortogen and Chlor-Trimeton Maleate in the Treatment of Allergic Conjunctivitis. Hanser, S. A.: Tr. Am. Acad. Ophth. **58**: 133, 1954.

Forty patients with simple allergic conjunctivitis were treated locally every four hours with a suspension containing 2.5 per cent Cortogen and 1.25 per cent Chlor-Trimeton. Nineteen patients served as controls and were treated locally with distilled water, buffer solution, Cortogen, Zephiran and epinephrine 1:1000, or Chlor-Trimeton. Eosinophil counts were made from lid scrapings. The Cortogen and Chlor-Trimeton eye-drop mixture produced a greater fall in the eosinophil count of the scrapings and a better symptomatic result than did any of the other compounds. M. C.

Miscellaneous Allergies

A Comparison of Leukocyte Lysis With Certain Other Immunologic Phenomena Demonstrable in Sera of Tuberculous Rabbits. Waksman, B. H., and Bocking, D.: Am. Rev. Tuberc. **69**: 1002, 1954.

Rabbits were sensitized intradermally or intravenously with BCG or with heat-killed human type tubercle bacilli. In lysis tests Old Tuberculin (OT) was used in dilutions of 1:5 and 1:20. Purified protein derivative (PPD) was used in concentrations of 5 and 50 gamma per milliliter in saline. Saline or a dilution of tuberculin (0.1 ml.) was incubated with 0.4 ml. of test blood or with 0.2 ml. of test serum plus 0.2 ml. of fresh, normal rabbit blood. The average percentage fall in leukocyte counts in the tubes containing tuberculin and saline were compared. Differences of less than 10 per cent were considered insignificant. It was found that the addition of OT or PPD to blood of tuberculin-sensitized rabbits resulted in lysis of leukocytes, which occurred over the course of several hours, but was most marked after six hours of incubation. Lymphocytes and polymorphonuclear cells were both involved in this lysis, the latter more rapidly and to a greater degree. No correlation

was found between the degree of skin reactivity to tuberculin and the lytic property of the serum. The lytic property could be destroyed in some, but not in all, antisera by heating at 57° C. for four hours. The lytic property was moderately well correlated with the presence of erythrocyte-agglutinating antibody to the tuberculin but was not correlated with a precipitating or complement-fixing antibody. A fall in lymphocyte counts six hours following the intravenous administration of tuberculin to tuberculin-sensitive rabbits could not be demonstrated when the sera from these rabbits were studied in vitro. The lytic property in rabbit serum differed in thermostability from that found in the sera of tuberculous guinea pigs and mice. It also differed in the type of cell affected and in the speed of lysis from the lytic antibody found in rabbits sensitized to ovalbumin and bovine gamma globulin. E. W.

The Cytology of the Tuberculin Reaction in Skin Windows in Man. Rebuck, J. W., and Yates, J. L.: Am. Rev. Tuberc. **69**: 216, 1954.

Experimental lesions were prepared by scraping the epithelium from a small area of the volar surface of the forearm. A tuberculin preparation was applied topically to the denuded surface. The lesion was covered with a sterile coverslip, overlaid with a square of sterile cardboard, and the entire area was then surmounted by surgical adhesive tape. Cells migrated to the undersurface of the coverslip within the first hour. The coverslip was removed, air-dried, and stained as a blood smear. Another coverslip was placed over the lesion and the process was repeated at timed intervals throughout the first, second, and occasionally the third day of the inflammatory reaction. Five lesions in subjects with negative cutaneous tuberculin reactions and nine lesions in tuberculin-positive subjects were studied. Old Tuberculin (OT) and purified protein derivative (PPD) were used in these experiments.

Histologic studies of the tuberculin-negative sites showed that there was a pronounced migration of neutrophilic leukocytes in the first two to eight-hour responses. At eight to twelve hours, the lymphocytes appeared in increasing numbers. The neutrophils showed marked degenerative changes in the twelve- to fourteen-hour studies and, in the same period, the lymphocytes underwent moderate cytoplasmic hypertrophy. At this point, the hypertrophying lymphocytes developed structural changes in both nucleus and cytoplasm which rendered them indistinguishable from tissue macrophages. From twelve to forty-eight hours, the presence of macrophages in the local inflammatory site was concurrent with a clearing of the experimental lesions.

In subjects with positive tuberculin reactions, there were marked alterations in the leukocytic sequences in the lesions. These resulted in defective and retarded mononuclear responses, which were due to depression of lymphocytic participation at various stages in the inflammatory responses. In two groups, outright lymphocytic deficit led to macrophage or neutrophilic accentuation for twenty-four hours, covering the period of normal lymphocytic participation. In a third group, early lymphocytic migration was replaced by a second migration of neutrophils supplanting macrophage predominance at twenty-four hours. E. W.

The Influence of Streptococcal Toxin on the Development of Tuberculin Sensitivity in Guinea Pigs. Grey, R. C., and Long, D. A.: Brit. J. Exper. Path. **35**: 85, 1954.

Tuberculin sensitivity was measured by the intracutaneous tuberculin reaction in guinea pigs sensitized with BCG or with dead virulent tubercle bacilli. When a group of these animals was treated with twenty-one daily in-

jections of streptococcal toxin, a threefold increase in tuberculin sensitivity resulted. This enhancing effect of streptococcal toxin could be prevented by heating the toxin prior to its injection or by pretreating the animals with scarlatinal antitoxin before toxin administration. Filtrates from a number of different strains of hemolytic streptococci were capable of increasing tuberculin sensitivity, regardless of their erythrogenic toxin content. Treatment with toxins derived from organisms other than hemolytic streptococci failed to increase tuberculin sensitivity. In the streptococcal toxin-treated guinea pigs, cortisone had approximately one-half its usual suppressive effect on tuberculin sensitivity.

The authors offer these findings in support of the "hypothesis that the hemolytic streptococcus initiates rheumatic fever by establishing a low-grade focus of infection associated with hypersensitivity of the tuberculin type to streptococcal allergens, that mesenchymal cells already damaged by streptococcal toxin show heightened susceptibility to streptococcal allergens and increased resistance to desensitization by naturally produced cortisone."

B. S.

Nature and Prevention of Local Skin Lesions From Insulin Administration. Observations on 100 Patients. Farbykant, M., and Ashe, B. I.: Metabolism **3**: 1, 1954.

A group of 100 diabetic patients under treatment with various insulin preparations were observed over a ten-month period with respect to skin lesions at the injection sites. Local lesions, consisting of inflammatory reactions, subcutaneous indurations, or lipodystrophies, developed in 75 per cent of these patients. Inflammatory lesions, which were characterized by itching, stinging or burning, tenderness, redness, and swelling, occurred most frequently. They developed within a few minutes to twelve hours after injection, reached a maximal intensity in six to twelve hours, and subsided in one to seven days. They occurred most frequently in patients who injected themselves improperly by inserting the needle at an acute angle to the skin. In forty-two patients, when the technique of injection was changed so that the needle was introduced perpendicularly into stretched skin sites which were changed daily, no local reactions appeared.

Skin tests with insulin on diabetic patients affected with local skin reactions and on nondiabetic controls revealed no significant differences in skin reactivity. Positive passive transfer reactions could not be obtained with the sera of patients who developed local skin lesions.

These findings indicate that local skin reactions to insulin preparations are usually nonspecific in nature and result from mechanical and chemical irritation induced by poor technique in the administration of insulin. M. C.

Death From Corticotrophin. Hill, B. H. R., and Swinburn, P. D.: Lancet **1**: 1218, 1954.

A case of acute anaphylactic shock following an intramuscular injection of 25 units of bovine corticotrophin which ended fatally is discussed. The patient was a 27-year-old man who had been suffering from an undiagnosed generalized dermatitis for three months. He was hospitalized and was given 10 units of porcine ACTH every six hours for twenty-seven consecutive days and then 25 units every six hours for the next six days. The rash improved somewhat and the patient was discharged from the hospital. The next day he received an injection of ACTH at a clinic and suddenly developed a slight reaction which was so mild as to require no specific therapy. Nine months later

the patient was readmitted to the hospital for treatment of his dermatitis which had again flared up. He was given 25 units of bovine corticotrophin and ten minutes later developed severe shock. He went into an acute vasomotor collapse for one-half hour and then temporarily responded to various supportive measures for several days before finally succumbing eight days later. According to the autopsy report, the patient was said to have died from brain damage secondary to the cerebral anoxia which had occurred during anaphylactic shock. Passive transfer tests with the patient's serum yielded negative reactions to Antuitrin-S and to bovine ACTH, but a positive reaction to porcine ACTH. Other patients treated with the same batch of ACTH developed no unusual reactions. In view of the negative passive transfer reaction to bovine ACTH, the authors are of the opinion that their patient died because of an acute anaphylactic reaction to ACTH of a nonspecific type.

R. W.

Insulin-Resistant Diabetes After Total Pancreatectomy. Report of a Case. Dituri, B.: New England J. Med. **251**: 13, 1954.

Diabetes mellitus which follows total pancreatectomy in man is relatively mild. In the absence of infection or complications, the requirement for insulin is usually stable and ranges from 20 to 40 units daily. Insulin-resistant diabetes after total pancreatectomy was encountered in a 50-year-old man. After operation, the patient's insulin requirements gradually increased from 20 to 180 units of insulin daily. Even this large amount of insulin was inadequate to control either the hyperglycemia or the glycosuria. Various changes in the amount, type, and time of injection of insulin, and intake of food failed to abolish glycosuria. Dosages of insulin which exceeded 180 units daily caused symptoms of hypoglycemia late in the evening. Blood studies indicated that 60 units of NPN insulin and 40 units of regular insulin had no effect on the blood glucose levels for the first six hours. After that, there was a precipitous drop in the blood glucose which was accompanied by many of the signs of impending insulin shock. When insulin was withheld from the patient, the secondary hypoglycemia did not occur. Serum samples collected one hour before and one hour after the morning dose of insulin and also approximately halfway between the daily doses of insulin, on a day when a total of 150 units of insulin was given, indicated that an immunologic mechanism was the cause of the unexplained resistance to insulin. The antibody titer was highest in the morning when there was little response of the blood glucose level to insulin and lowest later in the evening when the blood glucose had fallen to its lowest level. The problem of insulin resistance is briefly reviewed.

E. W.

The Effect of Cortisone on BCG Infection in the Guinea Pig. Birkhaug, K.: Am. Rev. Tuberc. **69**: 511, 1954.

Tuberculin-negative guinea pigs were given intramuscular injections of freshly prepared BCG vaccine. A control group of animals received the same dose of heated BCG. Some animals in each group were given cortisone acetate intramuscularly on alternate days for three months. The tissue response to OT one month after vaccination was significantly less in the cortisone-treated animals than in the untreated controls. The degree of sensitization was generally greater in the animals inoculated with living BCG than in those inoculated with killed BCG. In the cortisone-treated animals, the BCG papular reaction resulting from the diagnostic BCG test performed by the skin puncture method was faintly pink and scarcely raised above the skin surface, while

in the untreated group the papule was deeply reddish brown, markedly indurated, and presented a suppurating elevated center. Although the papular reaction was almost healed in the cortisone-treated animals within a week, it persisted for approximately one month in the control animals and healed in six to eight weeks after inoculation. The intradermal spread of vital dye was significantly less in cortisone-treated animals than in the controls, but no difference existed between the spread of dye in animals vaccinated with living or killed BCG. The eosinophil content of the circulating blood was significantly depressed after one week of hormone treatment and completely depressed after four weeks of treatment. Similarly, the absolute number of circulating lymphocytes diminished significantly in the hormone-treated animals. The absolute number of circulating monocytes and the monocyte-lymphocyte ratio significantly increased in the hormone-treated animals. Necropsy material from BCG-sensitized animals treated with cortisone showed a significant reduction of hyperplasia in regional and distal lymph nodes and in the spleen, a marked adrenal atrophy, but no sign of exacerbation of BCG lesions. Cortisone treatment during the active period of sensitization with BCG produced a significant increase in specific resistance against a challenge infection, which was most marked in animals sensitized with living BCG. E. W.

Fatality Following Penicillin Injection. Fisher, S.: Ann. Int. Med. **40**: 1227, 1954.

A fatal penicillin reaction which occurred in a patient with a negative allergic background is reported. A healthy 28-year-old man entered the hospital for a minor surgical procedure. He was given a low spinal anesthetic with procaine. After completion of the surgical procedure he received a prophylactic intramuscular injection of 300,000 units of aqueous penicillin. Within five minutes, he complained of chest pain and dyspnea. A few seconds later he became cyanotic and went into shock. Death ensued, despite all emergency measures. The autopsy revealed little of significance.

It was found that the patient had received penicillin previously on several occasions for minor illnesses without ill effects. There was a history that on two different occasions he had had such severe local reactions to Novocain that the intended operative procedure had been postponed. J. S.

Near-Fatal Shock From PAS Followed by Guillain-Barrés Syndrome. Bulley, K. G.: Am. Rev. Tuberc. **69**: 455, 1954.

Near-fatal shock associated with Guillain-Barrés syndrome caused by PAS was reported in a 29-year-old housewife with pulmonary tuberculosis. This patient received sodium para-aminosalicylic acid (PAS), 4 Gm. three times a day by mouth, and dihydrostreptomycin, 1 Gm. intramuscularly twice a week, without evidence of allergy for ten days. At this point, an intrapleural pneumonolysis was performed and the patient received PAS for three consecutive days in doses of 4 Gm. at breakfast only. On each occasion the administration of the drug was followed by severe headache, nausea, chills, malaise, and a temperature elevation to 102° F. The administration of PAS was discontinued. Approximately a week later, on her own initiative, the patient again took 4 Gm. of PAS. Within ten minutes she developed severe headache, nausea, vomiting, cramping pains in the abdomen and legs, and diarrhea. Severe pain in the back, chills, blurred vision, and conjunctival injection developed, followed by a generalized erythematous rash and shock. Large doses of analgesics, infusions of saline and plasma, epinephrine, antihistaminics, and Cortone, as well as oxygen, were administered over a two-

day period. Although there was marked improvement in her shocklike state, the patient developed bilateral facial palsy and paresis of both legs and arms. Neurological examination revealed bilateral paralysis of the facial nerves, absence of deep tendon and abdominal reflexes, bilateral peroneal foot drop. There was evidence of posterior column involvement and a diagnosis of Guillain-Barrés neuromyelo-radiculo-neuritis was made. On intensive vitamin and physiotherapy over an eighteen-month period, this patient made a gradual and almost complete recovery of muscle and nerve functions. E. W.

Four Untoward Reactions to Sodium Dehydrocholate, Including Two Fatal Cases. Sanchez, G. C., and Morris, L. E.: New England J. Med. **251**: 646, 1954.

In heart-lung preparations and in intact laboratory animals, bile salts can produce bradycardia and hypotension. Untoward reactions to sodium dehydrocholate were noted in four patients in whom the drug was used to study the circulation time. Two patients died as a result of the administration of this drug. The first, a 15-year-old girl with a large aortic-pulmonary arterial shunt, hypertrophy of right ventricle, and advanced pulmonary endoarteritis, died within forty minutes following the administration of sodium dehydrocholate. Death in this patient was attributed to marked pulmonary hypotension which precipitated syncope and subsequent death. The death of the second patient, a 50-year-old man with severe arterial sclerosis, myocardial and pulmonary infarctions, fibrinous pericarditis, an old thrombosis of the abdominal aorta, and bilateral hydrothorax, was attributed to myocardial ischemia produced by the stress of the injection. The third patient, a 46-year-old man with heart disease and equivocal congestive failure, went into shock which was attributed to the hypotensive and bradycardiac effect of sodium dehydrocholate in an unduly susceptible person. The fourth patient, a 69-year-old man with no previous history of allergic disease, was given sodium dehydrocholate in order to study the cardiovascular status prior to a prostatectomy. Three minutes following completion of the test, he became acutely dysnpeic, tachypneic, and had a shaking chill. There was a rise in his blood pressure and temperature, cyanosis of the nail beds, and sibilant rhonchi throughout both lung fields. Treatment consisted of the administration of oxygen, Demerol, Benadryl, and aminophylline. There was rapid improvement in this patient's condition. This reaction was attributed to hypersensitivity. It is suggested that patients with a history of allergy, or those with right to left shunts, may be particularly vulnerable to the untoward effects of sodium dehydrocholate. E. W.

Anaphylaxis

Some Quantitative Aspects of Passive Anaphylaxis in Pertussis-Vaccinated Mice. Pittman, M., and Germuth, F. G., Jr.: Proc. Soc. Exper. Biol. & Med. **87**: 425, 1954.

Mice were given intraperitoneal injections of pertussis vaccine and three days later were inoculated intravenously with varying amounts of antibovine serum albumin. After forty-eight hours, each mouse was given a small amount of crystalline bovine serum albumin intravenously. Nonvaccinated mice served as controls. In another experiment, histamine susceptibility of control vaccinated mice was determined by injecting intraperitoneally a small dose of histamine on the day of anaphylactic test.

A significant increase in susceptibility to passive anaphylaxis and to histamine was found in pertussis-vaccinated mice. The anaphylactic response could be graded in relation to the amount of antibody N injected, and reproducible titrations of the SD_{50} were obtained. In nonvaccinated mice, a low incidence of poorly graded anaphylactic shock was obtained. The histamine susceptibility of the animals could also be graded in relation to the amount of pertussis vaccine used, but this factor did not apply in passive anaphylaxis. Contrary to previous reports that a time interval of more than six hours between antibody and antigen administration was impractical, the writers demonstrated comparable anaphylactic sensitivity when sensitization was performed as long as forty-eight hours before antigen administration. These studies also indicate that mice treated with pertussis vaccine may be used to advantage in anaphylaxis experiments. M. C.

Pharmacology, Physiology, and Pathology

Changes in Plasma Levels of 17 Hydroxycorticosteroids During the Intravenous Administration of ACTH. I. A Test of Adrenocortical Capacity in the Human. Eik-Nes, K., Sandberg, A. A., Nelson, D. H., Tyler, F. H., and Samuels, L. T.: J. Clin. Invest. **33**: 1502, 1954.

A continuous intravenous infusion of ACTH was administered over a six-hour period to thirty-nine normal subjects and to six subjects with adrenal insufficiency. Plasma 17-hydroxycorticosteroid levels and eosinophil counts were made. Maximal stimulation of the adrenal cortex was obtained by doses of 15 to 20 I.U. of ACTH. When a 25 I.U. dose was given over a two-hour period, the plasma levels reached no greater peak than when the same dose was administered over an eight-hour period. Maximal adrenal stimulation occurred after six hours and plasma steroid levels remained unchanged at this level as long as ACTH was given. Readings returned to normal within six hours after the infusion was stopped. Six different preparations of ACTH all showed similar capacity to elicit adrenal stimulation regardless of animal source or technique of preparation. The U.S.P. assay is evidently adequate. In subjects having clinical symptoms of adrenal insufficiency there was little or no rise in steroid levels.

In normal individuals, plasma 17-hydroxycorticosteroid levels showed the greatest rise during the first two hours of the infusion. Eosinophil levels, on the other hand, showed no significant decrease (over 50 per cent) until four hours after the infusion was started. In one case, after a major surgical operation, the eosinophil level was too low to respond to an ACTH test, although plasma levels of 17-hydroxycorticosteroids increased in response to ACTH.

It is proposed that plasma 17-hydroxycorticosteroid levels measured over a six-hour period during ACTH infusion be used as the test of choice for evaluating adrenocortical capacity in man. K.

The Effects of Histamine-Liberators on the Mast Cells of the Rat. Riley, J. F.: J. Path. & Bact. **65**: 471, 1953.

Lethal doses of various chemical histamine-liberators were injected intravenously in rats. Two of these substances, stilbamidine and 2-hydroxy stilbamidine, because of their fluorescence in ultraviolet light, could readily be detected in the tissues. On histologic examination of fresh tissue spreads from these animals, the fluorescent material was found to be concentrated in the tissue mast cells and subsequently led to their disruption. Further observa-

tions by the author suggest that there is "a direct effect by the histamine-liberators on mast cells." This effect is prevented by premedication with an antihistamine. The author believes that, in addition to releasing heparin, the mast cells are also a source of histamine. J. S.

The Effect on Respiration of the Occlusion of a Bronchus in Man During Bronchospirometry. Pump, K. K.: J. Clin. Invest. **33**: 611, 1954.

Thirty-four patients with pulmonary tuberculosis were subjected to bronchospirometry. Recordings were made of each of the lungs. One lung was blocked either by clamping the catheter leading to it or by administering pure nitrogen while the opposite lung received oxygen. Blocking one lung at the end of the expiration immediately increased the tidal volume, respiratory rate, and functional residual capacity in the unblocked lung. Blocking one lung at the peak of a forced inspiration decreased the contralateral functional residual capacity and slowed (or at least did not increase) the respiratory rate. Tidal volume was likely to increase. There was considerable individual variation and the phenomena just described at times could be induced in one, but not in the other, lung of the same individual. The changes occurred prior to any changes in oxygenation. It is suggested that these observations were due to the Hering-Breuer reflex which depends on stretch receptors in the lung parenchyma. K.

Mechanism by Which Histamine Stimulates ACTH Release in Rats. Semonson, C. P., and Sawyer, C. H.: Am. J. Physiol. **177**: 405, 1954.

Subcutaneously administered histamine induced a 40 per cent drop in the eosinophil count one hour after injection into intact anesthetized rats. This eosinopenia was maintained for at least four hours. When the histamine was injected into anesthetized adrenal demedullated rats, the one-hour eosinopenic response did not occur, but the four-hour examination revealed the anticipated drop. When the potent antiadrenergic agent, SKF-501, and the non-adrenergic blocking analogue, D-ol, were injected twenty-four hours prior to the subcutaneous injections of histamine, the one-hour response was again absent, but the four-hour response was unaltered. When intravenous and subcutaneous injections of histamine were given simultaneously, a 20 per cent eosinopenia was produced in demedullated animals at one hour and a marked drop at four hours. Similar levels were noted in demedullated rats after pretreatment with D-ol.

When histamine was injected subcutaneously into unanesthetized demedullated rats, the eosinophil counts were similar to those following injections of saline. These findings demonstrate that subcutaneously administered histamine is not a natural or universal trigger mechanism in the stress response but acts rather in a nonspecific manner. Its effect on the hypophysis is mediated, at least in part, through the adrenal medulla, whereas intravenous histamine may act directly on the hypophysis. F.

Inhibition by Cortisone of the Binding of New Histamine in Rat Tissues. Schayer, R. W., Smiley, R. L., and Davis, K. J.: Proc. Soc. Exper. Biol. & Med. **87**: 590, 1954.

Cortisone-treated rats were given C^{14} L-histidine intraperitoneally and were sacrificed twenty-four hours later. The shaved abdominal skin was removed and analyzed for C^{14} histamine by isotope dilution. Following cor-

tisone, a marked drop in the C^{14} histamine bound in the skin resulted. The mechanism by which cortisone inhibits the rate of binding of new histamine in rat skin is not known. M. C.

Mechanism of the Potentiating Action of β-Diethylaminoethyl Diphenylpropylacetate. Axelrod, J., Reichenthal, J., and Brodie, B. B.: J. Pharmacol. & Exper. Therap. **112**: 49, 1954.

The drug, β-diethylaminoethyl diphenylpropylacetate HCl (SKF 525-A), is known to prolong the effectiveness of a variety of drugs. In rats, mice, and dogs, the biologic half-life and duration of action of these drugs were markedly prolonged by SKF 525-A. In the case of ephedrine, plasma levels one hour after the intraperitoneal administration of ephedrine with SKF 525-A were 6.0 mg. per liter, while the plasma levels of demethylated ephedrine (nor-ephedrine) were under 1.0 mg. per liter. Five hours after drug administration, ephedrine levels were still over 2 mg. per liter and nor-ephedrine levels were well under 1.0 mg. When ephedrine was injected alone, the one-hour level was slightly over 1.5 mg. per liter and the nor-ephedrine level was over 3.0 mg. per liter. Between the third and fourth hours the ephedrine level became zero and the nor-ephedrine level remained over 3.0 mg. per liter.

K.

Immediate Blood Cell Count Response to Epinephrine in Splenectomized Dogs. Hamilton, L. H., and Horvath, S. M.: Am. J. Physiol. **178**: 58, 1954.

When large doses of epinephrine are administered intravenously to splenectomized dogs, the blood cellular responses may vary from those found in normal animals. By means of catheters placed in the aorta, caudal vena cava, and the right ventricle, blood samples were withdrawn at intervals following the intravenous administration of epinephrine. Normal animals responded to intravenous adrenalin with an erythrocytosis, whereas the splenectomized dogs failed to do so. The white cell counts were similar in both groups for the first two minutes, but for the next three minutes the leukocyte response in splenectomized animals was somewhat lower than that in the normal animals. These findings suggest that the spleen possesses some control over the leukocyte response, but the mechanism involved is not known.

F.

Miscellaneous

Studies of Diphtheria Antitoxin in Rheumatic Fever Subjects: Analysis of Reactions to the Schick Test and of Antitoxin Responses Following Hyperimmunization With Diphtheria Toxoid. Kuhns, W. J., and McCarty, M.: J. Clin. Invest. **33**: 759, 1954.

Because rheumatic fever subjects show increased titers for streptococcal antigens, it became of interest to determine whether these patients show an exaggerated antibody response to other antigens, such as diphtheria toxoid. Schick tests and antitoxin responses were carried out on young persons convalescing from rheumatic fever or on those who gave a previous history of rheumatic fever, and on controls. Positive Schick reactions were obtained in 43 per cent of 104 rheumatic subjects and in 57 per cent of 91 controls. Following diphtheria immunization, the antitoxin responses of both groups were quantitatively similar, as were the immediate skin responses to Schick test material in individuals initially negative on Schick testing. Antistreptolysin

O titers were not significantly increased in either group following the injection of diphtheria toxoid. The ability to form nonprecipitating antitoxin was not found to be unusual in rheumatic patients. K.

Influence of Somatotrophic Hormone and Hydrocortisone Acetate on the Production of Hemolytic Antibodies in the Rat. Hoene, R., Rindani, T. H.: and Heuser, G.: Am. J. Physiol. **177**: 19, 1954.

Rats treated for seven days with hydrocortisone, STH (somatotrophic or growth hormone), or a combination of the two, were then injected with sheep erythrocytes. Hemolysin titers done on the fourth, seventh and tenth days following sensitization revealed a delay in the appearance and a reduction in the levels of the hemolytic antibody in those animals pretreated with either hydrocortisone or STH. Rats which received a combination of the two hormones had higher antibody levels than those treated with only one of the hormones. The somatotrophic hormone produced an increase in the size of the lymphatic organs (spleen and thymus) which, along with the simultaneous decrease in antibody levels, suggests that the antibodies are stored in these organs and are released by the administration of hydrocortisone. Therefore, in order to permit an optimal level of circulating antibodies, it is necessary to equilibrate the catabolic and anabolic hormones against each other. F.